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## Search History

Today's Date: 9/30/2000

| <u>DB Name</u> | <u>Query</u>             | <u>Hit Count</u> | <u>Set Name</u> |
|----------------|--------------------------|------------------|-----------------|
| USPT           | L4 and immortal\$        | 26               | <u>L5</u>       |
| USPT           | L3 and (oncogene or myc) | 89               | <u>L4</u>       |
| USPT           | dorsal root gangli\$     | 424              | <u>L3</u>       |
| USPT           | dorsal root gangli?      | 267              | <u>L2</u>       |
| USPT           | dorsal(w)root(w)gangli?  | 0                | <u>L1</u>       |

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| Set | Items | Description               |
|-----|-------|---------------------------|
| S1  | 41261 | DORSAL(W) ROOT(W) GANGLI? |
| S2  | 603   | S1 AND (ONCOGENE OR MYC)  |
| S3  | 0     | S2 AND IMMORAL?           |
| S4  | 0     | S2 AND IMMORTAL           |
| S5  | 34    | S2 AND IMMORTAL?          |
| S6  | 15    | RD (unique items)         |
| ?   |       |                           |

Dialog

file: medicine

9/30/00

amb

| Set | Items | Description                 |
|-----|-------|-----------------------------|
| S1  | 41261 | DORSAL (W) ROOT (W) GANGLI? |
| S2  | 134   | S1 AND IMMORTAL?            |
| S3  | 17    | S2 AND T(W) ANTIGEN         |
| S4  | 8     | RD (unique items)           |
| ?   |       |                             |

*Dialog*

*file: medicine*

*9/30/00*

*amb*

6/3,AB/1 (Item 1 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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12037841 BIOSIS NO.: 199900318360

Immortalized human dorsal root ganglion cells differentiate into neurons with nociceptive properties.

AUTHOR: Raymon Heather K(a); Thode Silke; Zhou Jiuying; Friedman Glenn C; Pardinas Jose R; Barrere Christian; Johnson Randolph M; Sah Dinah W Y  
AUTHOR ADDRESS: (a)Signal Pharmaceuticals Incorporated, 5555 Oberlin Drive, Suite 100, San Diego, CA, 92121\*\*USA

1999

JOURNAL: Journal of Neuroscience 19 (13):p5420-5428 July 1, 1999

ISSN: 0270-6474

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

ABSTRACT: A renewable source of human sensory neurons would greatly facilitate basic research and drug development. We had established previously conditionally **immortalized** human CNS cell lines that can differentiate into functional neurons (Sah et al., 1997). We report here the development of an **immortalized** human **dorsal root ganglion** (DRG) clonal cell line, HD10.6, with a tetracycline-regulatable **v-myc oncogene**. In the proliferative condition, HD10.6 cells have a doubling time of 1.2 d and exhibit a neuronal precursor morphology. After differentiation of clone HD10.6 for 7 d in the presence of tetracycline, **v-myc** expression was suppressed, and >50% of the cells exhibited typical neuronal morphology, stained positively for neuronal cytoskeletal markers, and fired action potentials in response to current injection. Furthermore, this cell line was fate-restricted to a neuronal phenotype; even in culture conditions that promote Schwann cell or smooth muscle differentiation of neural crest stem cells, HD10.6 differentiated exclusively into neurons. Moreover, differentiated HD10.6 cells expressed sensory neuron-associated transcription factors and exhibited capsaicin sensitivity. Taken together, these data indicate that we have established an **immortalized** human DRG cell line that can differentiate into sensory neurons with nociceptive properties. The cell line HD10.6 represents the first example of a human sensory neuronal line and will be valuable for basic research, as well as for the discovery of novel drug targets and clinical candidates.

6/3,AB/2 (Item 2 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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11450522 BIOSIS NO.: 199800231854

Proliferation and differentiation properties of permanent Schwann cell lines immortalized with a temperature-sensitive oncogene.

AUTHOR: Thi Anh Do; Evrard Claudine; Rouget Pierre(a)  
AUTHOR ADDRESS: (a)Lab. Biologie Moleculaire Differentiation, Unite Genetique Oncologiques, CNRS-URA 1967, Inst. Gu\*\*France

1998

JOURNAL: Journal of Experimental Biology 201 (6):p851-860 March, 1998

ISSN: 0022-0949

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: Permanent Schwann cells lines have been established in culture after stable transfection of newborn rat Schwann cells with the pJC-SVLTtsA vector, expressing a thermosensitive **oncogene** driven by the early promoter-enhancer region of the gliotropic GS/B variant of the papovavirus JC. The proliferation and differentiation of two clonal cell lines have been studied. The cells of these lines display the morphology

of primary Schwann cells and express Schwann cell differentiation markers such as the S-100 protein, laminin, the low-affinity receptor to nerve growth factor and the glial fibrillary acidic protein. One of the lines is able to differentiate further. Indeed, in the presence of **dorsal root ganglion** neurones, the cells synthesize the myelin Po protein and are capable of some myelination, although to a lesser extent than secondary Schwann cells.

6/3,AB/3 (Item 3 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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09948654 BIOSIS NO.: 199598403572

**Differential localization of cytoplasmic myosin II isoforms A and B in avian interphase and dividing embryonic and immortalized cardiomyocytes and other cell types in vitro.**

AUTHOR: Conrad Abigail H(a); Jaffredo Thierry; Conrad Gary W  
AUTHOR ADDRESS: (a)Div. Biol., Ackert Hall, Kansas State Univ., Manhattan, KS 66506-4901\*\*USA

1995

JOURNAL: Cell Motility and the Cytoskeleton 31 (2):p93-112 1995

ISSN: 0886-1544

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

ABSTRACT: Two principal isoforms of cytoplasmic myosin II, A and B (CMIIA and CMIIB), are present in different proportions in different tissues. Isoform-specific monoclonal and polyclonal antibodies to avian CMIIA and CMIIB reveal the cellular distributions of these isoforms in interphase and dividing embryonic avian cardiac, intestinal epithelial, spleen, and **dorsal root ganglia** cells in primary cell culture. Embryonic cardiomyocytes react with antibodies to CMIIB but not to CMIIA, localize CMIIB in stress-fiber-like-structures during interphase, and markedly concentrate CMIIB in networks in the cleavage furrow during cytokinesis. In contrast, cardiac fibroblasts localize both CMIIA and CMIIB in stress fibers and networks during interphase, and demonstrate slight and independently regulated concentration of CMIIA and CMIIB in networks in their cleavage furrows. V-myc -immortalized cardiomyocytes, an established cell line, have regained the ability to express CMIIA, as well as CMIIB, and localize both CMIIA and CMIIB in stress fibers and networks in interphase cells and in cleavage furrows in dividing cells. Conversely, some intestinal epithelial, spleen, and **dorsal root ganglia** interphase cells express only CMIIA, organized primarily in networks. Of these, intestinal epithelial cells express both CMIIA and CMIIB when they divide, whereas some dividing cells from both spleen and **dorsal root ganglia** express only CMIIA and concentrate it in their cleavage furrows. These results suggest that within a given tissue, different cell types express different isoforms of CMII, and that cells expressing either CMIIA or CMIIB alone, or simultaneously, can form a cleavage furrow and divide.

6/3,AB/4 (Item 1 from file: 34)  
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci  
(c) 2000 Inst for Sci Info. All rts. reserv.

04352043 Genuine Article#: RX766 Number of References: 37

**Title: GENETIC INSTABILITY OF CHROMOSOME-3 IN HPV- IMMORTALIZED AND TUMORIGENIC HUMAN KERATINOCYTES**

Author(s): MONTGOMERY KD; TEDFORD KL; MCDUGALL JK

Corporate Source: FRED HUTCHINSON CANC RES CTR,CANC BIOL GRP,C1-015,1124 COLUMBIA ST/SEATTLE//WA/98104

Journal: GENES CHROMOSOMES & CANCER, 1995, V14, N2 (OCT), P97-105

ISSN: 1045-2257

Language: ENGLISH Document Type: ARTICLE

Abstract: The HPV-1811 cell line is derived from primary human foreskin keratinocytes that have been transfected with human papilloma virus type 18. At late passage, these cells produce invasive squamous cell carcinomas when injected into nude mice. A striking, but unstable, aberration of chromosome 3 occurs very early after establishment of the culture; a consistent rearrangement is observed concomitant with tumorigenicity. Using molecular cytogenetic techniques, we characterized the complex development of this aberration. A whole chromosome probe to this chromosome was made by linker-adaptor PCR amplification of a single flow-sorted chromosome. Hybridization of this probe to normal metaphase chromosomes revealed the der (3) to be composed of chromosome 3, distal 13q, and 21q22. Hybridization of a 3q subtelomeric probe and a glycoprotein V probe which maps to 3qter indicated that this locus is duplicated in the final form of the chromosome, but that much instability occurs prior to its establishment. The ETS2 **oncogene**, which maps to 21q22, is translocated to the der(3) when the cell line becomes tumorigenic, but not prior to this time. Early-passage cells which have been induced to become tumorigenic by exposure to the carcinogen nitrosomethylurea also have the localization of the ETS2 at 3qter. (C) 1995 Wiley-Liss, Inc.

6/3,AB/5 (Item 2 from file: 34)

DIALOG(R)File 34:SciSearch(R) Cited Ref Sci  
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04129967 Genuine Article#: RG584 Number of References: 43

**Title: DIFFERENTIAL LOCALIZATION OF CYTOPLASMIC MYOSIN-II ISOFORMS-A AND ISOFORMS-B IN AVIAN INTERPHASE AND DIVIDING EMBRYONIC AND IMMORTALIZED CARDIOMYOCYTES AND OTHER CELL-TYPES IN-VITRO**

Author(s): CONRAD AH; JAFFREDO T; CONRAD GW

Corporate Source: KANSAS STATE UNIV AGR & APPL SCI, DIV BIOL, ACKERT  
HALL/MANHATTAN//KS/66506; CNRS, INST EMBRYOL CELLULAIRE & MOLEC/F-94736  
NOGENT-SUR MARNE//FRANCE/; COLL FRANCE/NOGENT SUR MARNE//FRANCE/

Journal: CELL MOTILITY AND THE CYTOSKELETON, 1995, V31, N2, P93-112

ISSN: 0886-1544

Language: ENGLISH Document Type: ARTICLE

Abstract: Two principal isoforms of cytoplasmic myosin II, A and B (CMIIA and CMIIB), are present in different proportions in different tissues. Isoform-specific monoclonal and polyclonal antibodies to avian CMIIA and CMIIB reveal the cellular distributions of these isoforms in interphase and dividing embryonic avian cardiac, intestinal epithelial, spleen, and **dorsal root ganglia** cells in primary cell culture. Embryonic cardiomyocytes react with antibodies to CMIIB but not to CMIIA, localize CMIIB in stress-fiber-like-structures during interphase, and markedly concentrate CMIIB in networks in the cleavage furrow during cytokinesis. In contrast, cardiac fibroblasts localize both CMIIA and CMIIB in stress fibers and networks during interphase, and demonstrate slight and independently regulated concentration of CMIIA and CMIIB in networks in their cleavage furrows. V-myc - **immortalized** cardiomyocytes, an established cell line, have regained the ability to express CMIIA, as well as CMIIB, and localize both CMIIA and CMIIB in stress fibers and networks in interphase cells and in cleavage furrows in dividing cells. Conversely, some intestinal epithelial, spleen, and **dorsal root ganglia** interphase cells express only CMIIA, organized primarily in networks. Of these, intestinal epithelial cells express both CMIIA and CMIIB when they divide, whereas some dividing cells from both spleen and **dorsal root ganglia** express only CMIIA and concentrate it in their cleavage furrows. These results suggest that within a given tissue, different cell types express different isoforms of CMII, and that cells expressing either CMIIA or CMIIB alone, or simultaneously, can form a cleavage furrow and divide. (C) 1995 Wiley-Liss, Inc.

6/3,AB/6 (Item 3 from file: 34)

DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

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02086977 Genuine Article#: KA058 Number of References: 64

Title: **NEUROBLASTOMA X SPINAL-CORD (NSC) HYBRID CELL-LINES RESEMBLE DEVELOPING MOTOR NEURONS**

Author(s): CASHMAN NR; DURHAM HD; BLUSZTAJAN JK; ODA K; TABIRA T; SHAW IT; DAHROUGE S; ANTEL JP

Corporate Source: MCGILL UNIV, MONTREAL NEUROL INST, DEPT NEUROL & NEUROSURG, 3801 UNIV ST/MONTREAL H3A 2B4/QUEBEC/CANADA/; BOSTON UNIV, SCH MED, DEPT PATHOL/BOSTON//MA/02118; NATL INST NEUROSCI, NCNP/TOKYO 187//JAPAN/

Journal: DEVELOPMENTAL DYNAMICS, 1992, V194, N3 (JUL), P209-221

ISSN: 1058-8388

Language: ENGLISH Document Type: ARTICLE

Abstract: We have developed a series of mouse-mouse neural hybrid cell lines by fusing the aminopterin-sensitive neuroblastoma N18TG2 with motor neuron-enriched embryonic day 12-14 spinal cord cells. Of 30 neuroblastoma-spinal cord (NSC) hybrids displaying a multipolar neuron-like phenotype, 10 express choline acetyltransferase, and 4 induce twitching in cocultured mouse myotubules. NSC-19, NSC-34, and their subclones express additional properties expected of motor neurons, including generation of action potentials, expression of neurofilament triplet proteins, and acetylcholine synthesis, storage, and release. In addition, NSC-34 cells induce acetylcholine receptor clusters on cocultured myotubes, and undergo a vimentin-neurofilament switch with maturation in culture, similar to that occurring in neuronal development. NSC cell lines appear to model selected aspects of motor neuron development in an **immortalized** clonal system.

6/3,AB/7 (Item 4 from file: 34)

DIALOG(R) File 34:SciSearch(R) Cited Ref Sci

(c) 2000 Inst for Sci Info. All rts. reserv.

01568447 Genuine Article#: HH589 Number of References: 48

Title: **ESTABLISHMENT OF AN OSTEOGENIC CELL-LINE DERIVED FROM ADULT-MOUSE BONE-MARROW STROMA BY USE OF A RECOMBINANT RETROVIRUS**

Author(s): MATHIEU E; SCHOETERS G; VANDERPLAETSE F; MERREGAERT J

Corporate Source: UNIV INSTELLING ANTWERP, DEPT BIOCHEM, BIOTECHNOLAB/B-2610 WILRIJK//BELGIUM/; UNIV INSTELLING ANTWERP, DEPT BIOCHEM, BIOTECHNOLAB/B-2610 WILRIJK//BELGIUM/; CEN SCK, DEPT RADIOPROTECT/B-2400 MOL//BELGIUM/

Journal: CALCIFIED TISSUE INTERNATIONAL, 1992, V50, N4 (APR), P362-371

Language: ENGLISH Document Type: ARTICLE

Abstract: In order to characterize fibroblastic colony-forming units (CFU-F) from murine bone marrow in relation to osteogenesis, adherent cells of 7-day-old BALB/c mouse bone marrow cultures were infected with a recombinant retrovirus (N2/DELTA-fosB) containing the bacterial neomycin resistance gene. One of the G418-resistant clones, MN7, was selected for further analysis on the basis of its high expression of the bone-specific alkaline phosphatase. The cells have now been in culture for more than 1 year and maintain a stable phenotype. The osteogenic nature of the **immortalized** clone MN7 was demonstrated as follows: (1) Mineralization was detected by Sr-85 uptake and with the Von Kossa staining method only after in vitro cultivation on a collagen type I matrix. (2) Osteoblastic phenotype markers, including the synthesis of type I collagen, osteonectin, and the bone-specific isoenzyme of alkaline phosphatase were expressed in vitro. (3) MN7 cells responded to bone effectors such as parathyroid hormone and 1,25-dihydroxyvitamin D3. (4) Intraperitoneal injection of MN7 cells into 1-day-old BALB/c mice produced typical osteosarcomas in all animals. We conclude that MN7, derived entirely in vitro from a stromal CFU-F colony, represents a stable murine osteosarcoma cell line expressing the osteoblastic phenotype and provides the first direct evidence needed to establish adult mouse marrow-derived, nonhematopoietic stromal cells as osteoprogenitors.

6/3,AB/8 (Item 1 from file: 35)  
DIALOG(R)File 35:Dissertation Abstracts Online  
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01324763 AAD9334496

**AN IMMORTALIZED CLONAL RAT SCHWANN CELL LINE (SEAD): EXPRESSION OF  
NEUROTROPHIC FACTORS AND MYELIN PROTEINS**

Author: IMPERATO, EILEEN LOUISE

Degree: PH.D.

Year: 1993

Corporate Source/Institution: THE UNIVERSITY OF ROCHESTER (0188)

Source: VOLUME 54/07-B OF DISSERTATION ABSTRACTS INTERNATIONAL.

PAGE 3493. 223 PAGES

The neurotrophic factors, nerve growth factor (NGF) and insulin-like growth factor 1 (IGF-1), are important in peripheral nerve regeneration and are expressed in activated Schwann cells in vivo. Because Schwann cells proliferate slowly in vitro, we sought to create a permanently growth stimulated Schwann cell population. Therefore, we established and characterized a genetically engineered **immortalized** clonal Schwann cell line (SEAD) from primary rat Schwann cells by gene transfer of the **oncogene** 12S ELA using a retroviral vector. SEAD cells showed an 8-fold increase in mitotic index compared to primary Schwann cells and, like primary Schwann cells, were immunoreactive for S-100, vimentin, glial fibrillary acidic protein (GFAP), IGF-1, and NGF-receptor (low affinity, 192 IgG). This is the first example of in vitro staining of IGF-1 in both Schwann cells and SEAD cells. SEAD cell lysates also were immunoreactive for NGF protein as determined by enzyme-linked immunosorbent assay. Mitomycin C (MC), an antimitotic agent, decreased NGF-receptor and NGF immunoreactivity in SEAD cells; however, there was no effect on S-100, vimentin, GFAP or IGF-1 immunoreactivity. MC arrested SEAD cell proliferation but was completely reversible following removal of MC and a brief recovery period. SEAD cells also were immunoreactive for myelin proteins, P<sub>0</sub> and myelin basic protein (MBP), and Northern analysis revealed mRNA for both P<sub>0</sub> and MBP. However, when co-cultured with **dorsal root ganglion** neurons, SEAD cells did not associate with or myelinate these neurons. SEAD cells showed no growth in soft agar but form Schwannoma-like masses when injected into nude mice. These results suggest that primary and genetically altered Schwann cells express trophic factors important for peripheral nerve regeneration. Additionally, SEAD cells represent an **immortalized** rat clonal Schwann cell line that has the potential for further investigation into Schwann cell gene regulation. For example, SEAD cells express the myelin proteins, P<sub>0</sub> and MBP, and may offer a unique model system for studies of the role of these proteins in myelination. Finally, SEAD cells lend themselves well to studies of the state of Schwann cell proliferation.

6/3,AB/9 (Item 1 from file: 73)  
DIALOG(R)File 73:EMBASE  
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10531229 EMBASE No: 1999415837

**Overexpression of activated neu/erbB2 initiates immortalization and  
malignant transformation of immature Schwann cells in vitro**

Sherman L.; Sleeman J.P.; Hennigan R.F.; Herrlich P.; Ratner N.

L. Sherman, Department of Cell Biology, Neurobiology and Anatomy, Univ.  
Cincinnati College of Medicine, 231 Bethesda Avenue, Cincinnati, OH  
45267-0521 United States

Oncogene ( ONCOGENE ) (United Kingdom) 18 NOV 1999, 18/48 (6692-6699)

CODEN: ONCNE ISSN: 0950-9232

DOCUMENT TYPE: Journal; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 57

The neu/erbB2 protooncogene is overexpressed in numerous human cancers



and is mutationally activated in N-ethyl-N-nitrosourea (ENU)-induced rodent tumors of the Schwann cell lineage. We investigated whether expression of activated neu in Schwann cells is sufficient to initiate their **immortalization** and transformation. Clones of embryonic **dorsal root ganglia** cells infected with a retrovirus bearing activated neu (NID cells) were selected based on their expression of Schwann cell-specific markers. Compared to embryonic Schwann cells infected with a virus encoding empty vector, we found that NID cells have altered shapes and disorganized cytoskeletons, grow in the absence of growth factors required for normal Schwann cell survival and proliferation, and can be repeatedly passaged. Furthermore, NID cells are invasive in an in vitro matrix invasion assay and form metastatic tumors when injected into syngeneic animals. The neu-induced growth and invasive phenotypes could be reversed by drugs that inhibit Ras and Src activity. Interestingly, later stage Schwann cells infected with activated neu failed to become **immortalized**. These findings indicate that constitutive activation of erbB2 is sufficient to initiate the **immortalization** and transformation of immature Schwann cells, and support the notion that Schwann cells have particular developmental stages during which they are susceptible to **immortalizing** and transforming events.

6/3,AB/10 (Item 1 from file: 98)  
DIALOG(R)File 98:General Sci Abs/Full-Text  
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03546290 H.W. WILSON RECORD NUMBER: BGSI97046290  
**Regulators of apoptosis on the road to persistent alphavirus infection.**  
Griffin, Diane E  
Hardwick, J. Marie  
Annual Review of Microbiology (Annu Rev Microbiol) v. 51 ('97) p. 565-92  
SPECIAL FEATURES: bibl il ISSN: 0066-4227  
LANGUAGE: English  
COUNTRY OF PUBLICATION: United States  
WORD COUNT: 14517

**ABSTRACT:** Alphavirus infection can trigger the host cell to activate its genetically programmed cell death pathway, leading to the morphological features of apoptosis. The ability to activate this death pathway is dependent on both viral and cellular determinants. The more virulent strains of alphavirus induce apoptosis with increased efficiency both in animal models and in some cultured cells. Although the immune system clearly plays a central role in clearing virus, the importance of other cellular factors in determining the outcome of virus infections are evident from the observation that mature neurons are better able to resist alphavirus-induced apoptosis than immature neurons are, both in culture and in mouse brains. These findings are consistent with the age-dependent susceptibility to disease seen in animals. Cellular genes that are known to regulate the cell death pathway can modulate the outcome of alphavirus infection in cultured cells and perhaps in animals. The cellular bax and bak genes, which are known to accelerate cell death, also accelerate virus-induced apoptosis. In contrast, inhibitors of apoptotic cell death such as bcl-2 suppress virus-induced apoptosis, which can facilitate a persistent virus infection. Thus, the balance of cellular factors that regulate cell death may be critical in virus infections. Additional viral factors also contribute to this balance. The more virulent strains of alphavirus have acquired the ability to induce apoptosis in mature neurons, while mature neurons are resistant to cell death upon infection with less virulent strains. Here we discuss a variety of cellular and viral factors that modulate the outcome of virus infection. Reprinted by permission of the publisher.

6/3,AB/11 (Item 1 from file: 155)  
DIALOG(R)File 155:MEDLINE(R)  
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10067774 99398501

**Overexpression of Akt (protein kinase B) confers protection against apoptosis and prevents formation of ceramide in response to pro-apoptotic stimuli.**

Goswami R; Kilkus J; Dawson SA; Dawson G

Department of Pediatrics and Biochemistry and Molecular Biology,  
University of Chicago, Chicago, Illinois 60637, USA.

Journal of neuroscience research (UNITED STATES) Sep 15 1999, 57 (6)  
p884-93, ISSN 0360-4012 Journal Code: KAC

Contract/Grant No.: R01-NS-36866, NS, NINDS; P01-HD-09402, HD, NICHD

Languages: ENGLISH

Document type: JOURNAL ARTICLE

An immortalized dorsal root ganglion cell line F-11 exhibits many properties of spinal cord neurons and undergoes apoptosis in response to growth factor withdrawal and the exogenous addition of inhibitors of phosphatidylinositol-3-kinase (PI3K). To elucidate the mechanism of apoptosis we generated F-11 clones which overexpressed either the p110 subunit of PI3K, a constitutively active form of protein kinase B/Akt (Myristoylated Akt), or a dominant-negative form (c-Akt). The first two constructs were protective against apoptosis induced by PI3K inhibitors such as wortmannin and LY294002. Caspase-3 (CPP32) levels peaked at 4 hr to 6 hr in response to pro-apoptotic drugs, and this increase was attenuated by 50% in F-11 with constitutively active Akt. The Akt protection was confirmed by DNA fragmentation studies. Both neo-transfected and the c-Akt dominant-negative transfected F-11 cells showed increased ceramide formation (twofold) in response to staurosporine, wortmannin, or LY294002; whereas cells with a constitutively active Akt (Myr-Akt) showed no increase in ceramide when treated with staurosporine, wortmannin, or LY294002. Ceramide was a more potent activator of CPP32 and an inducer of apoptosis when added as the native form (hydroxy- or nonhydroxy-), rather than the more water-soluble C(2)-ceramide. Overexpression of PI3K (p110) and Akt protected cells against ceramide-induced apoptosis, suggesting that Ceramide action is upstream of Akt in these cells and suggesting that Akt might be a target for inhibition by ceramide. Both staurosporine and C(2)-ceramide activated the Jun kinase (JNK) cascade and C(2)-ceramide increased caspase-3 (CPP32) activity in cells expressing wild-type c-Jun, but not dominant-negative (TAM-67) c-Jun. We suggest that this pathway is also involved in apoptosis, consistent with the idea that ceramide has multiple kinase and kinase-modulating targets in the apoptotic pathway of neurons. J. Neurosci. Sci. 57:884-893, 1999. Copyright 1999 Wiley-Liss, Inc.

6/3,AB/12 (Item 1 from file: 159)

DIALOG(R)File 159:Cancerlit

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01143052 96605376

**Transcriptional activation and repression mediated through the MYC transcription factor network (Meeting abstract).**

Ayer DE; Hurlin P; Queva C; Lawrence Q; Eisenman RN

Div. of Basic Sciences, Fred Hutchinson Cancer Research Center, Seattle, WA

J Cell Biochem; Suppl 19A:3 1995 ISSN 0730-2312

Languages: ENGLISH

Document Type: MEETING ABSTRACTS

**Myc** proteins are members of the bHLHZip class of transcription factors and are important in proliferation, apoptosis and differentiation. Max is a bHLHZip protein which is an obligate partner for **Myc** function. **Myc** and Max form sequence-specific DNA binding heterocomplexes. Mad is another bHLHZip protein which can compete with **Myc** by forming heterocomplexes with Max. Mad:Max complexes repress, while **Myc**:Max complexes activate, transcription from promoter constructs. We have shown that the Mad protein is rapidly induced upon differentiation of several myeloid cell lines. During differentiation a switch from **Myc**:Max heterocomplexes to Mad:Max heterocomplexes is observed. Similar results have been obtained for differentiation of primary human keratinocytes. HPV immortalized

keratinocytes also induce Mad upon differentiation, but rare, non-differentiating variants, fail to express Mad. Thus induction of Mad is closely linked to differentiation in at least two distinct cell lineages. We have also detected Mad expression in the dorsal root ganglia and restricted regions of the neural tube in early (E10) mouse embryos. These expression patterns are also suggestive of a role in differentiation. The switch from Myc:Max to Mad:Max complexes may reflect the repression of transcription of Myc-regulated genes by Mad. To understand how Mad functions as a repressor we searched for additional protein-protein interactions. We have found that Mad and Mx1, but not Myc or Max, specifically interact with two homologues (mSin3A and B) of the S cerevisiae repressor protein Sin3. The mSin:Mad association is mediated through one of four paired amphipathic helix domains in mSin3 and a potential amphipathic helix located in the N-terminal portion of Mad. Furthermore, the mSin:Mad complex can interact with Max, through the Mad bHLHZip region, and bind DNA as a ternary complex. Point mutations within the Mad N-terminal helix disrupt interactions with mSin3 and inhibit Mad mediated repression in vivo. We speculate that Mad may function as a negative regulator of gene expression in association with Max by tethering a novel mammalian repressor to specific DNA binding sites. Because Max is expressed constitutively and capable of interacting with several key regulatory proteins we explored the possibility that Max might interact with additional, as yet uncharacterized, proteins. We therefore employed Max as 'bait' in a yeast two hybrid screen of a mouse embryonic cDNA library. Four unique Max-interacting bHLHZip proteins were identified as well as each of the known Max partners. Additional cloning and sequence analysis revealed that these constituted four novel bHLHZip proteins. Two of the proteins appear to be related to Mad primarily in their bHLHZip domains. The other two proteins are not members of either the Mad or Myc families but possess proline- and glutamine-rich segments reminiscent of transcriptional activation regions. These clones have tissue-specific expression patterns and appear to be differentially expressed during embryonic development and cell differentiation. Max appears to be at the center of a network of transcription factors whose activities and levels may be key determinants of cell behavior.

6/3,AB/13 (Item 1 from file: 442)  
DIALOG(R) File 442:AMA Journals  
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00113781  
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**The Molecular Basis for Understanding Neurotrophins and Their Relevance to Neurologic Disease (ARTICLE)**

KERNIE, STEVEN G.; PARADA, LUIS F.  
Archives of Neurology  
May, 2000; Basic Science Seminars in: tzn654  
LINE COUNT: 00302

The field of neurotrophin biology has made great advances in recent years to include a greater understanding of signaling pathways and broader understanding of the diverse biological roles of these molecules. This review will focus primarily on the nerve growth factor family of neurotrophins and how recent descriptions of the molecular function of both the ligands and the receptors have helped us to understand the basis for many neurologic processes. Ultimately, the goals of such studies are to give us further insight into potential diagnostic and therapeutic uses for these factors or signaling intermediates that may activate given pathways in neurotrophin signaling to achieve a particular objective based upon the underlying disease.

6/3,AB/14 (Item 2 from file: 442)  
DIALOG(R) File 442:AMA Journals

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00111076

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**Life and Death in Otolaryngology Mechanisms of Apoptosis and Its Role in the Pathology and Treatment of Disease (ARTICLE)**

MOSTAFAPOUR, SAM P.; HOCKENBERY, DAVID M.; RUBEL, EDWIN W  
Archives of Otolaryngology  
July, 1999; Review Article: tzo729  
LINE COUNT: 01001

Objectives: To review recent advances in our understanding of programmed cell death, or apoptosis, and discuss implications of these basic science advances in our understanding of causes and potential treatments of a variety of diseases of the head and neck. Data Sources: Basic science literature relevant to the study of apoptosis and its clinical implications. Conclusions: Apoptosis is now understood to be important in the normal development and survival of all multicellular organisms. Deregulation of this normally tightly controlled process underlies a variety of disease states, including neoplasia, autoimmune disease, and disorders of the central nervous system. A better understanding of this process and its regulation may help otolaryngologists better understand diseases relevant to this specialty and will lead to improved therapeutic interventions. Arch Otolaryngol Head Neck Surg. 1999;125:729-737

6/3,AB/15 (Item 1 from file: 444)  
DIALOG(R) File 444:New England Journal of Med.  
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00111206

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**Association Between High Levels Of Expression Of The TRK Gene And Favorable Outcome In Human Neuroblastoma (Original Articles)**

Nakagawara, Akira; Arima-Nakagawara, Miwako; Scavarda, Nancy J.; Azar, Christopher G.; Cantor, Alan B.; Brodeur, Garrett M.  
The New England Journal of Medicine  
Mar 25, 1993; 328 (12),pp 847-854  
LINE COUNT: 00473 WORD COUNT: 06533

**Abstract**

**Background and Methods.** The nerve growth factor receptor is expressed in some neuroblastomas, in which its primary component is encoded by the TRK proto-oncogene. To determine the relation of the expression of TRK messenger RNA in neuroblastomas to other clinical and laboratory variables, we studied frozen tumor samples from 77 patients. In addition, we tested two primary neuroblastomas that expressed TRK for responsiveness to nerve growth factor.

**Results.** TRK expression strongly correlated with favorable tumor stage (I, II, and IVS vs. III and IV), younger age (<1 year vs. greater/= 1 year), normal N-myc copy number, and low level of N-myc expression. N-myc amplification (indicated by a high copy number) correlated with advanced tumor stage, older age, an adrenal site of the primary tumor, low level of expression of TRK, and high level of expression of N-myc. Analysis of five-year cumulative-survival rates demonstrated an association of a very favorable outcome with a high level of TRK expression (86 percent vs. 14 percent) and with normal N-myc copy number (84 percent vs. 0 percent). Univariate analysis showed that these two variables were the most powerful predictors of outcome (chi-square = 51.30, P<0.001; and chi-square = 93.61, P<0.001, respectively). TRK expression still had significant prognostic value when the analysis was restricted to tumors without N-myc amplification. In primary cultures of neuroblastoma cells expressing TRK, exposure to nerve growth factor induced early gene expression and neurite

outgrowth, but deprivation of nerve growth factor led to neuronal cell death.

Conclusions. A high level of expression of the TRK proto-oncogene in a neuroblastoma is strongly predictive of a favorable outcome. A tumor with a functional nerve growth factor receptor may be dependent on the neurotrophin nerve growth factor for survival and may regress in its absence, allowing a new approach to the treatment of certain patients with neuroblastoma. (N Engl J Med 1993;328:847-54).

3/3,AB/1 (Item 1 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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Dialog (file: medicine)

6/1/01

amb

13038039 BIOSIS NO.: 200100245188

**Gene expression profile of F-11 tumor cells whose expression of GD3-synthase is suppressed.**

AUTHOR: Zeng Guichao(a); Gao Luoyi(a); Yu Rebert K(a)

AUTHOR ADDRESS: (a)Medical College of Georgia, 1120 15th Street, CB-2803, Augusta, GA, 30912\*\*USA

JOURNAL: FASEB Journal 15 (4):pA193 March 7, 2001

MEDIUM: print

CONFERENCE/MEETING: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001 Orlando, Florida, USA March 31-April 04, 2001

ISSN: 0892-6638

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

**ABSTRACT:** We have established a subclone of the rat **dorsal root ganglion** -derived F-11 cells whose expression of ganglioside GD3 is inhibited by stable transfection of the antisense vector against GD3-synthase gene. In the antisense-transfected F-11 cells, the level of ganglioside GD3 greatly decreased while ganglioside GM3, the **precursor** of GD3, was accumulated. Characterization of the cell line showed that down-regulation of GD3 expression correlated with the reduction in cell migration and invasion in vitro and tumor growth and metastasis in vivo. We also found that the reduced tumor growth and metastasis of the GD3-suppressed F-11 cells in nude mice resulted from minimal angiogenesis of the tumors through down-regulation of the VEGF expression. To identify genes involved in the altered behaviors of the tumor cells resulting from the suppression of ganglioside GD3 expression, we analyzed gene expression profiles of the antisense-transfected F-11 cells and the control untransfected and the sense-transfected F-11 cells using DNA microarrays consisting of 8,800 genes. The results showed that 104 and 171 genes were expressed differently between the antisense-transfected F-11 cells and the control untransfected F-11 cells and the sense-transfected F-11 cells, respectively. Ten genes were commonly upregulated and twenty genes down-regulated in both the untransfected F-11 cells and the sense-transfected F-11 cells. These genes likely represent candidates for cell growth, apoptosis or carcinogenesis.

2001

3/3,AB/2 (Item 2 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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12881030 BIOSIS NO.: 200100088179

**Sensory neuron development in the absence of NT-3 signaling.**

AUTHOR: Patel T D(a); Kucera J; Snider W D

AUTHOR ADDRESS: (a)Univ N Carolina, Chapel Hill, NC\*\*USA

JOURNAL: Society for Neuroscience Abstracts 26 (1-2):pAbstract No-3201 2000

MEDIUM: print

CONFERENCE/MEETING: 30th Annual Meeting of the Society of Neuroscience New Orleans, LA, USA November 04-09, 2000

SPONSOR: Society for Neuroscience

ISSN: 0190-5295

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

**ABSTRACT:** NT-3 is required for the survival of proprioceptive DRG neurons

during embryonic development. In addition, mice lacking NT-3 exhibit a 70% reduction in the number of DRG neurons due to a deficiency in all DRG neuronal classes. Whether this global deficiency is due to regulation of apoptosis or an effect of NT-3 on **precursor** proliferation has been controversial. In order to explore the role of NT-3 in regulating ganglion cell number and proprioceptive neuron development, we crossed NT-3 deficient mice with mice carrying a targeted deletion of the proapoptotic BCL-2 homologue BAX. Elimination of BAX resulted in a 60% increase in the number of DRG neurons over wild type controls even in the absence of NT-3. Furthermore, the Bax/NT-3 double null mice exhibited a comparable increase in the number of dorsal root axons projecting to the spinal cord. At both E15 and P0, parvalbumin positive axons could be seen entering the spinal cord of the double nulls and projecting toward the motor pools in the ventral horn. In contrast, peripheral axon counts in the nerve to the soleus muscle demonstrated a reduction in the number of large caliber axons, as well as the absence of parvalbumin stained axons in the periphery. In addition, muscle spindles failed to develop in the Bax/NT-3 double null mice. These findings demonstrate that the profound influence of NT-3 on DRG neuronal number is due entirely to the regulation of apoptosis. They further show that the initial collateralization of proprioceptive axons into the spinal cord is an NT-3 independent process. However, peripheral proprioceptive projections and their associated muscle spindles require NT-3 to develop normally.

2000

3/3,AB/3 (Item 3 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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12671613 BIOSIS NO.: 200000425115

**Cisplatin-induced apoptotic cell death in mouse hybrid neurons is blocked by antioxidants through suppression of cisplatin-mediated accumulation of p53 but not of Fas/Fas ligand.**

AUTHOR: Park Sun Ah; Choi Kyeong Sook; Bang Jung Hee; Huh Kyoony; Kim Seung U(a)

AUTHOR ADDRESS: (a)Division of Neurology, Department of Medicine,  
University Hospital, University of British Columbia, 2211 Wesbrook Mall,  
Vancouver, BC, V6T 2B5\*\*Canada

JOURNAL: Journal of Neurochemistry 75 (3):p946-953 Septmeber, 2000

MEDIUM: print

ISSN: 0022-3042

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

**ABSTRACT:** Peripheral neuropathy following cisplatin treatment is a major limiting factor in cisplatin chemotherapy of cancer patients. We investigated the pathomechanism underlying cisplatin neuropathy using a mouse **dorsal root ganglion** neuron-neuroblastoma hybrid cell line (N18D3) developed in our laboratory. DNA fragmentation, a characteristic feature of apoptosis, was induced in hybrid neurons following treatment with cisplatin. Accumulation of p53, Fas, and Fas ligand (Fas-L) was also demonstrated in these neurons. Preincubation with N-acetylcysteine (NAC), a **precursor** of glutathione, blocked cisplatin-induced apoptosis completely, whereas Trolox, a vitamin E analogue, blocked it partially. Cisplatin-induced p53 accumulation was suppressed by NAC treatment, whereas p53 accumulation was retarded by Trolox treatment. In contrast, neither NAC nor Trolox showed any inhibitory effect on cisplatin-induced Fas/Fas-L accumulation. These results suggest that the neuroprotective effects of antioxidants against cisplatin-induced neurotoxicity in hybrid neurons are mediated mainly through the inhibition of p53 accumulation but not of Fas/Fas-L accumulation by these antioxidants.

2000

3/3,AB/4 (Item 4 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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12399895 BIOSIS NO.: 200000153397

**Loss of brain-derived neurotrophic factor-dependent neural crest-derived sensory neurons in neurotrophin-4 mutant mice.**

AUTHOR: Liebl Daniel J; Klesse Laura J; Tessarollo Lino; Wohlman Todd;  
Parada Luis F(a)

AUTHOR ADDRESS: (a)Center for Developmental Biology, University of Texas  
Southwestern Medical Center, 6000 Harry Hines Boulevard, Dallas, TX,  
75235-9133\*\*USA

JOURNAL: Proceedings of the National Academy of Sciences of the United  
States of America. 97 (5):p2297-2302 Feb. 29, 2000

ISSN: 0027-8424

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

ABSTRACT: Peripheral ganglion neurons confer sensory information including touch, pain, temperature, and proprioception. Sensory modality is linked to specific neurotrophin (NTF) requirements. NT-3 supports survival of neurons that differentiate primarily into proprioceptors whereas nerve growth factor and brain-derived neurotrophic factor (BDNF) support subpopulations that transmit nociception and mechanoreception, respectively. We examined sensory neurons of gene-targeted mouse mutants at the NT-4, BDNF, NT-3, and TrkA loci. We show that NT-4 functions early in gangliogenesis, upstream of BDNF. In the absence of NT-4 function, BDNF-dependent, TrkB-expressing neurons fail to appear. The results are consistent with the model that **precursor** cells intended to become BDNF-dependent mechanoreceptors instead differentiate into NT-3-dependent proprioceptive neurons.

2000

3/3,AB/5 (Item 5 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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12393572 BIOSIS NO.: 200000147074

**Attenuation of cisplatin-induced apoptotic neuronal death by antioxidants in mouse hybrid neurons.**

AUTHOR: Park S A(a); Bang J H; Choi K S; Huh K(a); Kim S U(a)

AUTHOR ADDRESS: (a)Dept. of Neurology, Ajou University, Suwon\*\*South Korea

JOURNAL: Society for Neuroscience Abstracts. 25 (1-2):p1525 1999

CONFERENCE/MEETING: 29th Annual Meeting of the Society for Neuroscience.  
Miami Beach, Florida, USA October 23-28, 1999

SPONSOR: Society for Neuroscience

ISSN: 0190-5295

RECORD TYPE: Citation

LANGUAGE: English

SUMMARY LANGUAGE: English

1999

3/3,AB/6 (Item 6 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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12393150 BIOSIS NO.: 200000146652

**Effects of amyloid peptides on the expression of neuropeptides in dorsal root ganglion neurons. Relevance to chronic pain in aging?**

AUTHOR: Ma W(a); Zheng W-H(a); Kar S(a); Quirion R(a)



AUTHOR ADDRESS: (a) Douglas Hospital Research Center, McGill University,  
Montreal, PQ, H4H 1R3\*\*Canada  
JOURNAL: Society for Neuroscience Abstracts. 25 (1-2):p1434 1999  
CONFERENCE/MEETING: 29th Annual Meeting of the Society for Neuroscience.  
Miami Beach, Florida, USA October 23-28, 1999  
SPONSOR: Society for Neuroscience  
ISSN: 0190-5295  
RECORD TYPE: Citation  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
1999

3/3,AB/7 (Item 7 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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12338669 BIOSIS NO.: 200000092171

**Multiple polyphosphoinositide pathways regulate apoptotic signalling in a dorsal root ganglion derived cell line.**

AUTHOR: Goswami R; Dawson S A; Dawson G(a)

AUTHOR ADDRESS: (a) Department of Pediatrics, HM 4068, University of  
Chicago, 5821 S. Maryland Ave., Chicago, IL, 60637\*\*USA

JOURNAL: Journal of Neuroscience Research 59 (1):p136-144 Jan. 1, 2000

ISSN: 0360-4012

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

ABSTRACT: The polyphosphoinositides play important roles in transmembrane signalling but are also involved in anchoring cell surface proteins, organellar transport, cytoskeleton organization, and cell survival. The polyphosphoinositides synthesized by phosphatidylinositol-3 kinase (PI-3K), (Ptd(3,4)InsP2, and PtdIns(3,4,5)P3), appear to play a critical role in cell survival by membrane recruitment and activation of Akt kinase. Inhibitors of PI3K, wortmannin, and LY294002, induced a time-dependent activation of caspase-3 (CPP32), with a peak at 6 hr, leading to subsequent cell death by apoptosis in a **dorsal root ganglion cell line (F-11)**. Lowering cyclic AMP (cAMP) levels enhanced both caspase-3 activation and cell death induced by PI3K inhibitors, whereas a nonhydrolyzable cAMP analog (Bt2cAMP), lowered CPP32 and was protective. We stably transfected the F-11 cells with the constitutively active p110 catalytic subunit of PI-3 kinase and observed resistance to both caspase-3 (CPP32) activation and subsequent apoptosis induced by either wortmannin or LY294002. Treatment of F-11 cells with bradykinin (BK) stimulated the hydrolysis of a different polyphosphoinositide, PtdIns(4,5)P2, and enhanced both wortmannin-induced caspase-3 (CPP32) activation and subsequent apoptosis. PtdIns(4,5)P2 is also a **precursor** of the anti-apoptotic PtdIns(3,4,5)P3 and lowering cAMP levels with opioid agonists for 30 min enhanced both the hydrolysis of PtdIns(4,5)P2 and cellular apoptosis. The enhancement was opioid dose-dependent and opioid antagonist (naloxone)-reversible and was also seen following 24-hr exposure to opioids such as U69,593 and Dala2, Dleu5 enkephalin (DADLE). However, unlike the bradykinin stimulation of PtdIns(4,5)P2 hydrolysis following activation of phospholipase C, the opioid-enhanced hydrolysis was independent of external Ca<sup>2+</sup> and was blocked by pertussis toxin, suggesting a different mechanism involving G<sub>i</sub>, G<sub>o</sub>, or betagamma-subunits. In summary, both the receptor-mediated lowering of cAMP levels and the hydrolysis of 4,5-polyphosphoinositides have no direct effect on caspase-3 activity or apoptosis but do exacerbate the activation of caspase-3-like activity and subsequent cell death by apoptosis induced by inhibitors of 3-polyphosphoinositide synthesis. We suggest that multiple polyphosphoinositide pathways are involved in the regulation of apoptosis.

3/3,AB/8 (Item 8 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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12255702 BIOSIS NO.: 200000009204

**Immunohistochemical localization of kininogen in rat spinal cord and brain.**

AUTHOR: Li Zhaohong(a); Tyor William R(a); Xu Jian(a); Chao Julie; Hogan Edward L(a)

AUTHOR ADDRESS: (a)Department of Neurology, Medical University of South Carolina, Charleston, SC, 29425\*\*USA

JOURNAL: Experimental Neurology 159 (2):p528-537 Oct., 1999

ISSN: 0014-4886

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

**ABSTRACT:** Kininogen localization has been determined by immunocytochemistry in rat spinal cord and brain using a kinin-directed kininogen monoclonal antibody. In the spinal cord, there were immunostained neurons and fibers in laminae I, II, VII, and IX, intensely stained fibers in the superficial layers of the dorsal horn, and immunoreactive glial and endothelial cells. Small neurons, satellite cells, and Schwann cells immunostained distinctly in the **dorsal root ganglion**. In the brain stem, there were immunoreactive neurons and fibers in the tractus solitarius and nucleus, trigeminal spinal tract and nuclei, periaqueductal gray matter, vestibular nuclei, cochlear nuclei, trapezoid body, medial geniculate nucleus, and red nucleus. Immunostained neurons and fibers were also found in cerebellum (dentate nucleus), cerebral cortex (layers III and V), hippocampus (pyramidal cell layer), and corpus callosum. Glia and endothelial cells stained in all brain regions. The widespread location of kininogen in neurons and their processes, as well as in glial and endothelial cells, indicates more than one functional role, including those proposed as a mediator, a calpain inhibitor, and a kinin **precursor**, in a variety of neural activities and responses.

1999

3/3,AB/9 (Item 9 from file: 5)  
DIALOG(R)File 5:Biosis Previews(R)  
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12231188 BIOSIS NO.: 199900526037

**P0 and PMP22 mark a multipotent neural crest-derived cell type that displays community effects in response to TGF-beta family factors.**

AUTHOR: Hagedorn Lilian; Suter Ueli; Sommer Lukas(a)

AUTHOR ADDRESS: (a)Institute of Cell Biology, Swiss Federal Institute of Technology, ETH-Honggerberg, CH-8093, Zurich\*\*Switzerland

JOURNAL: Development (Cambridge) 126 (17):p3781-3794 Sept., 1999

ISSN: 0950-1991

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

**ABSTRACT:** Protein zero (P0) and peripheral myelin protein 22 (PMP22) are most prominently expressed by myelinating Schwann cells as components of compact myelin of the peripheral nervous system (PNS), and mutants affecting P0 and PMP22 show severe defects in myelination. Recent expression studies suggest a role of P0 and PMP22 not only in myelination but also during embryonic development. Here we show that, in dorsal root ganglia (DRG) and differentiated neural crest cultures, P0 is expressed in the glial lineage whereas PMP22 is also detectable in neurons. In addition, however, P0 and PMP22 are both expressed in a multipotent cell

type isolated from early DRG. Like neural crest stem cells (NCSCs), this P0/PMP22-positive cell gives rise to glia, neurons and smooth-muscle-like cells in response to instructive extracellular cues. In cultures of differentiating neural crest, a similar multipotent cell type can be identified in which expression of P0 and PMP22 precedes the appearance of neural differentiation markers. Intriguingly, this P0/PMP22-positive **progenitor** exhibits fate restrictions dependent on the cellular context in which it is exposed to environmental signals. While single P0/PMP22-positive **progenitor** cells can generate smooth muscle in response to factors of the TGF-beta family, communities of P0/PMP22-positive cells interpret TGF-beta factors differently and produce neurons or undergo increased cell death instead of generating smooth-muscle-like cells. Our data are consistent with a model in which cellular association of postmigratory multipotent progenitors might be involved in the suppression of a non-neural fate in forming peripheral ganglia.

1999

3/3,AB/10 (Item 10 from file: 5)  
DIALOG(R)File 5:BIOSIS Previews(R)  
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12037841 BIOSIS NO.: 199900318360

**Immortalized human dorsal root ganglion cells differentiate into neurons with nociceptive properties.**

AUTHOR: Raymon Heather K(a); Thode Silke; Zhou Jiuying; Friedman Glenn C; Pardinase Jose R; Barrere Christian; Johnson Randolph M; Sah Dinah W Y  
AUTHOR ADDRESS: (a)Signal Pharmaceuticals Incorporated, 5555 Oberlin Drive, Suite 100, San Diego, CA, 92121\*\*USA

JOURNAL: Journal of Neuroscience 19 (13):p5420-5428 July 1, 1999

ISSN: 0270-6474

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

**ABSTRACT:** A renewable source of human sensory neurons would greatly facilitate basic research and drug development. We had established previously conditionally immortalized human CNS cell lines that can differentiate into functional neurons (Sah et al., 1997). We report here the development of an immortalized human **dorsal root ganglion** (DRG) clonal cell line, HD10.6, with a tetracycline-regulatable v-myc oncogene. In the proliferative condition, HD10.6 cells have a doubling time of 1.2 d and exhibit a neuronal **precursor** morphology. After differentiation of clone HD10.6 for 7 d in the presence of tetracycline, v-myc expression was suppressed, and >50% of the cells exhibited typical neuronal morphology, stained positively for neuronal cytoskeletal markers, and fired action potentials in response to current injection. Furthermore, this cell line was fate-restricted to a neuronal phenotype; even in culture conditions that promote Schwann cell or smooth muscle differentiation of neural crest stem cells, HD10.6 differentiated exclusively into neurons. Moreover, differentiated HD10.6 cells expressed sensory neuron-associated transcription factors and exhibited capsaicin sensitivity. Taken together, these data indicate that we have established an immortalized human DRG cell line that can differentiate into sensory neurons with nociceptive properties. The cell line HD10.6 represents the first example of a human sensory neuronal line and will be valuable for basic research, as well as for the discovery of novel drug targets and clinical candidates.

1999

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| Set | Items | Description                |
|-----|-------|----------------------------|
| S1  | 24686 | DORSAL(W) ROOT(W) GANGLION |

?ds

| Set | Items | Description                      |
|-----|-------|----------------------------------|
| S1  | 24686 | DORSAL(W) ROOT(W) GANGLION       |
| S2  | 452   | S1 AND (PROGENITOR OR PRECURSOR) |
| S3  | 270   | RD (unique items)                |

Dialog (file: medicine)

6/1/01

amb